

**Remarks**

Entry of the foregoing and reconsideration of the application identified in caption as amended, pursuant to and consistent with the Rules of Practice in Patent Cases, and in light of the remarks which follow, is respectfully requested.

By the present amendment, claims 1, 5, 6, and 8 have been amended and claims 2-4, 7, and 9-13 have been deleted, so that claims 1, 5, 6, and 8 will be pending upon entry of the present amendment.

Regarding the amendment to the specification filed April 3, 2009, as stated therein, the text present in the claims, as originally filed, was added to the specification to preserve the original disclosure of the specification independent of subsequent claim revisions.

Claims 1-4, 7, 8, 11, and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by either of Raisfeld (US 4,507,321) or Charonis et al. (WO 94/12464) or Ilenchuk et al. (WO 99/51213).

Claims 1-4, 8, and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by either Eckart et al. (EP 0,884,046) or Hahn et al. (WO 96/23490).

Claims 3, 4, 8 and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by either Wolf et al. (WO 98/06376) or Matsubara et al. (JP 2003/113047).

Claims 3, 4, 7, 8, and 11-13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Minoshima et al. (JP 07/268,323). These rejections are respectfully traversed.

Rejected claims 1-4, 7, 8, and 11-13 are now represented by claims 1 and 8, as claims 2-4, 7, and 11-13 have been deleted. Further, claims 1 and 8 of the present invention have been amended and relate to a method for the cosmetic treatment of the human skin to improve hydration of the human skin and to maintain the beauty thereof by application of an oral composition containing from 0.25 to 0.5 mg or topical composition containing from 0.01 to 0.02 g/100 ml of the active principle. None of the cited prior art relates to a method of cosmetic treatment of the human skin to improve hydration of the human skin to maintain the beauty thereof.

Moreover, the experimental evidence reported in the present specification shows that such effect of the hydration, as measured by a corneometer, is achieved. The corneometer is an instrument for measuring stratum corneum moisture, that is the hydration of the outermost layer of the skin. It measures the electrical capacitance of the skin surface as

an indicator of stratum corneum hydration. The corneometer results in the study showed an increase in skin hydration with a statistically significant difference between the mean values observed after treatment and the corresponding values observed after the placebo. The degree of hydration, determined by electric capacitance measured with the corneometer, increased by over 10% with a high statistical significance ( $p < 0.001$ ). Further, the Rinaldi Declaration previously submitted shows that such effect of hydration is not obvious in view of a cell renewal effect as described by the prior art.

In contrast, Raisfeld, Charonis and Ilenchuk relate to the treatment of skin of a subject suffering from a pathological disorder or having damaged skin for cell regeneration processes in pathological or damaged skin. For instance, Raisfeld relates to treatments of skin disorders, such as wound healing, treating burns, treating ischemic, decubitus and peptic ulcers, plastic and reconstructive surgery, dermatological disorders, the treatment of psoriasis and retardation of fibrosis after injuries to the spinal cord and nervous system. As the Examiner notes, such prior art indicates that polyamines can stimulate or inhibit epithelial cell growth. This is a very broad indication indeed, which does not provide any teaching about improving hydration for cosmetic purposes. Neither novelty nor obviousness of the cosmetic treatment of instant claim 1 can be reasonably objected on the preceding teachings: a method of cosmetic treatment to improve hydration of the skin to maintain beauty is not made known or obvious by prior art describing a therapeutical treatment of pathological or damaged skin based on cell renewal or possibly even cell inhibition.

Moreover, it should be noted that, the inclusion of the claimed amounts of active principle rebuts the Examiner's position with respect to the alleged inherent effect of the active principle.

Raisfeld, Charonis, and Ilenchuk, describe that polyamines can both stimulate and inhibit epithelial cell growth. Such a disclosure cannot provide any teaching about improving skin hydration for cosmetic purposes, as confirmed by the expert Rinaldi.

Furthermore, it should be pointed out that amended claim 1, recites a range of 0.25 - 0.5 mg of spermidine trihydrochloride, which - by calculation - corresponds to approximately 0.02 - 0.04 % of free spermidine in an oral administration unit (such as the tablets of the examples). Example 10 of Raisfeld describes a capsule with 50 mg of spermidine, which amounts to 16.6% b.w. of that capsule. The use of such tablet is the same as the use indicated for Example 9 of Raisfeld, i.e., "to treat various injuries and disease

states in which an oral route of administration is desirable, e.g., peptic ulcers, burns and trauma, and inflammatory bowel diseases such as ulcerative colitis.”

On the other hand, Examples 1 and 2 of the present application describe a tablet for oral administration containing 0.25 mg of spermidine trihydrochloride, which amounts to 0.14 mg of free spermidine in the tablet, i.e., about 0.021% b.w. of free spermidine in the tablet. This is a concentration almost 800 times lower than that disclosed in Raisfeld. Therefore, the oral use of spermidine at a much higher concentration in a single oral administration unit to cure diseases, such as peptic ulcers and colitis does not suggest the above range as taught by the instant application.

Eckart shows how to enhance the photo protective activity of the active principles vitamins C and E on the skin irradiated with UV. Polyamines are only enhancers. Accordingly, the hydration improvement on non-irradiated skin resulting from the clinical study in the present application is therefore a different effect, as again explained in Dr. Rinaldi's Affidavit. Hahn does not relate to cosmetic treatment of human skin, rather it relates to animals for inhibiting skin irritation. Wolf does not relate to cosmetic treatment of human skin, rather it relates to a nail strengthening composition. Matsubara does not relate to cosmetic treatment of human skin, rather it relates to a hair cosmetic. Minoshima does not relate to cosmetic treatment of human skin, rather it relates to a pharmaceutical antioxidant preparation.

None of the cited documents of Eckart, Hahn, Wolf, Matsubara, or Minoshima describe or suggest that spermine and/or spermidine in free or salified form in the claimed amounts can be active as cosmetics inasmuch as they are able to withhold water at the stratum corneum of the epidermis, so that they can improve hydration of the human skin to maintain beauty in any subject.

Withdrawal of the record rejections noted above regarding Raisfeld, Charonis, Ilenchuk, Eckart, Hahn, Wolf, Matsubara, or Minoshima under 35 U.S.C. § 102(b) is respectfully requested.

Composition claims 3-13, now represented by method claims 5, 6, and 8, stand rejected under 35 U.S.C. § 103 as being obvious over Minoshima et al. (JP 07/268323) in view of Henderson (WO 00/37087), Ioannides (WO 02/15860) and Eckart et al. This rejection is respectfully traversed.

Applicant's submit that the rejection of composition claims 3-13 has been rendered moot in view of the amendment of claims 5, 6, and 8 to method claims which depend from method claim 1. These claims are patentable for the same reasons as that noted above with respect to claim 1.

Accordingly, withdrawal of the record rejection of Claims 5, 6, and 8 under 35 U.S.C. § 103 as being obvious over Minoshima et al. (JP 07/268323) in view of Henderson (WO 00/37087) and Ioannides (WO 02/15860) is respectfully requested.

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is hereby earnestly solicited.

Respectfully submitted,

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